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=> file registry

=> e memapsin
E1            3     MEMANTINE/BI
E2           73     MEMAP/BI
E3           11 --> MEMAPSIN/BI
E4            3     MEMAZIN/BI
E5            3     MEMAZINE/BI
E6           12     MEMB/BI
E7            4     MEMBANE/BI
E8            2     MEMBB/BI
E9            1     MEMBBRANE/BI
E10        4766     MEMBER/BI
E11           1     MEMBER1/BI
E12           4     MEMBERANE/BI

=> File .Biotech

=> s e3
L1          318 MEMAPSIN/BI

=> s (memapsin 2 or beta secretase or beta amyloid precursor protein or APP)
L2       758318 (MEMAPSIN 2 OR BETA SECRETASE OR BETA AMYLOID PRECURSOR PROTEIN
                OR APP)

=> s l1 and l2
L3          318 L1 AND L2

=> s (l2 or memapsin 2) and (OM 99 or OM-99 or dipeptide isostere or dipeptide or
isostere) and Alzheimer?
L4          354 (L2 OR MEMAPSIN 2) AND (OM 99 OR OM-99 OR DIPEPTIDE ISOSTERE
                OR DIPEPTIDE OR ISOSTERE) AND ALZHEIMER?

=> s l1 and l4
L5           55 L1 AND L4

=> s l5 and (computer program# or software program#)
L6           11 L5 AND (COMPUTER PROGRAM# OR SOFTWARE PROGRAM#)

=> s l6 and (recombinant?)
L7           10 L6 AND (RECOMBINANT?)

=> s l7 and (treat? or therapeut? or diagnos? or prevent? or inhibit?)
L8           10 L7 AND (TREAT? OR THERAPEUT? OR DIAGNOS? OR PREVENT? OR INHIBIT
                ?)

=> s Tang J?/au; s Hong L/au; s Ghosh A/au; s Koelsch G/au
L9        12110 TANG J?/AU


L10         586 HONG L/AU


L11        2290 GHOSH A/AU


L12         113 KOELSCH G/AU

=> s l8 and (l9 or l10 or l11 or l12)
L13           9 L8 AND (L9 OR L10 OR L11 OR L12)

=> d l13 1-9 bib ab

L13  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2006 ACS on STN
```

AN 2001:12489 CAPLUS
DN 134:80832
TI **Inhibitors** of **memapsin 2** and use thereof
IN **Tang, Jordan J. N.**; Hong, Ling; Ghosh, Arun K.
PA Oklahoma Medical Research Foundation, USA; The Board of Trustees of the University of Illinois
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000665	A2	20010104	WO 2000-US17742	20000627
	WO 2001000665	A3	20010927		
	WO 2001000665	C2	20020725		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2374346	AA	20010104	CA 2000-2374346	20000627
	AU 2000057735	A5	20010131	AU 2000-57735	20000627
	EP 1194449	A2	20020410	EP 2000-943236	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003506322	T2	20030218	JP 2001-507071	20000627
	US 6545127	B1	20030408	US 2000-604608	20000627
	EP 1496124	A1	20050112	EP 2004-9534	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002049303	A1	20020425	US 2001-796264	20010228
	US 2002164760	A1	20021107	US 2001-795903	20010228
	US 2002115600	A1	20020822	US 2001-845226	20010430
	US 2003199676	A1	20031023	US 2003-420044	20030417
	US 2004220079	A1	20041104	US 2004-773754	20040206
	US 2004167075	A1	20040826	US 2004-820953	20040408
	AU 2004202058	A1	20040610	AU 2004-202058	20040514
	AU 2004202059	A1	20040610	AU 2004-202059	20040514
PRAI	US 1999-141363P	P	19990628		
	US 1999-168060P	P	19991130		
	US 2000-177836P	P	20000125		
	US 2000-178368P	P	20000127		
	US 2000-210292P	P	20000608		
	US 2000-210306P	P	20000608		
	AU 2000-57715	A3	20000627		
	AU 2000-57735	A3	20000627		
	EP 2000-943208	A3	20000627		
	US 2000-603713	A3	20000627		
	US 2000-604608	A3	20000627		
	WO 2000-US17742	W	20000627		
	US 2000-752878	A1	20001228		
	US 2001-845226	A1	20010430		

AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one

analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Figure 1). The **inhibition** constant of OM99-2 is 1.6 x 10-9 M against **recombinant** pro-**memapsin 2**. Crystallog. of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using com. available **software programs** and techniques familiar to those in organic chemical and enzymol., to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:12487 CAPLUS
DN 134:68049
TI Catalytically active **recombinant memapsin 2**, 3D crystal structure based **inhibitor** design, synthesis, and screening, for **Alzheimer**'s disease **treatment**
IN **Tang, Jordan J. N.**; Lin, Xinli; Koelsch, Gerald
PA Oklahoma Medical Research Foundation, USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000663	A2	20010104	WO 2000-US17661	20000627
	WO 2001000663	A3	20011004		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2374610	AA	20010104	CA 2000-2374610	20000627
	AU 2000057715	A5	20010131	AU 2000-57715	20000627
	EP 1196609	A2	20020417	EP 2000-943208	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003503072	T2	20030128	JP 2001-507069	20000627
	US 6545127	B1	20030408	US 2000-604608	20000627
	EP 1496124	A1	20050112	EP 2004-9534	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002049303	A1	20020425	US 2001-796264	20010228
	US 2002164760	A1	20021107	US 2001-795903	20010228
	US 2002115600	A1	20020822	US 2001-845226	20010430
	US 2003199676	A1	20031023	US 2003-420044	20030417
	US 2004220079	A1	20041104	US 2004-773754	20040206
	US 2004167075	A1	20040826	US 2004-820953	20040408
	AU 2004202058	A1	20040610	AU 2004-202058	20040514
	AU 2004202059	A1	20040610	AU 2004-202059	20040514
PRAI	US 1999-141363P	P	19990628		
	US 1999-168060P	P	19991130		
	US 2000-177836P	P	20000125		

US 2000-178368P	P	20000127
US 2000-210292P	P	20000608
US 2000-210306P	P	20000608
AU 2000-57715	A3	20000627
AU 2000-57735	A3	20000627
EP 2000-943208	A3	20000627
US 2000-603713	A3	20000627
US 2000-604608	A3	20000627
WO 2000-US17661	W	20000627
US 2000-752878	A1	20001228
US 2001-845226	A1	20010430

AB A method for producing catalytically active **recombinant** **memapsin 2** comprising expression in a bacteria and refolding the **recombinant** **memapsin 2** under conditions which dissociate and then slowly refold the enzyme into a catalytically active form is disclosed. A method of isolating **inhibitors** of cleavage by **memapsin 2** comprising adding to one or more potential **inhibitors** of catalytically active **recombinant** **memapsin 2** , and a substrate for **memapsin 2**, and screening for decreased cleavage of the substrate by the **inhibitors**, wherein the **inhibitors** are in a library of small synthetic mols., like proteins and peptides. Alternatively, the **inhibitors** are oligonucleotides **preventing** or decreasing expression of catalytically active **memapsin 2**. A method for designing or obtaining **inhibitors** of catalytically active **memapsin 2** comprising modeling an **inhibitor** based on the crystallization coordinates of **memapsin 2** or parameters. A database comprising binding properties and chemical structures of compds. designed or screened by modeling an **inhibitor** based on the crystallization coordinates of **memapsin 2** or parameters is claimed. A method of **treating** or **preventing** **Alzheimer**'s disease comprising administering to a patient in need thereof an **inhibitor** of **memapsin 2** which binds to the active site of the **memapsin 2** defined by the presence of two catalytic aspartic residues and substrate binding cleft, is also claimed. The cDNAs of two new human membrane-associated aspartic proteases, **memapsin** 1 and **memapsin 2** , have been cloned and sequenced. The substrate and subsite specificity of the catalytically active enzyme have been determined The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Fig. 1). The **inhibition** constant of OM99-2 is 1.6 x 109 M against **recombinant** pro-**memapsin** **2**. Crystallog. of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used to design new **inhibitors**, using com. available **software programs** and techniques familiar to those in organic chemical and enzymol., to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 3 OF 9 USPATFULL on STN

AN 2004:280778 USPATFULL
TI **Inhibitors** of **Memapsin 2** and use thereof
IN Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, UNITED STATES (U.S. corporation)
The Board of Trustees of the University of Illinois, Urbana, IL, UNITED STATES (U.S. corporation)
PI US 2004220079 A1 20041104
AI US 2004-773754 A1 20040206 (10)
RLI Continuation of Ser. No. US 2001-845226, filed on 30 Apr 2001, ABANDONED
Division of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP Kenneth E. Jenkins Eqs., Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA, 94111-3834
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 4 OF 9 USPATFULL on STN
AN 2004:215966 USPATFULL
TI **Inhibitors** of **Memapsin 2** and use thereof
IN **Tang, Jordan J. N.**, Edmond, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, UNITED STATES (U.S. corporation)
The Board of Trustees of the University of Illinois, Urbana, IL, UNITED

STATES (U.S. corporation)
PI US 2004167075 A1 20040826
AI US 2004-820953 A1 20040408 (10)
RLI Continuation of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 5 OF 9 USPATFULL on STN
AN 2003:134541 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN **Tang, Jordan J. N.**, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK (U.S. corporation)
PI US 2003092629 A1 20030515
AI US 2001-32818 A1 20011228 (10)
PRAI US 2001-275756P 20010314 (60)
US 2000-258705P 20001228 (60)
DT Utility
FS APPLICATION
LREP HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
CLMN Number of Claims: 24
ECL Exemplary Claim: 1

DRWN 9 Drawing Page(s)
LN.CNT 2203
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed-, The substrate and subsite specificity of the catalytically active enzyme have been determined by a method which determines the initial hydrolysis rate of the substrates by using MALDI-TOF/MS. Alternatively, the subsite specificity of **memapsin** can be determined by probing a library of **inhibitors** with **memapsin 2** and subsequently detecting the bound **memapsin 2** with an antibody raised to **memapsin 2** and an alkaline phosphatase conjugated secondary antibody. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2.** The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2.** The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2.** Processes for the synthesis of substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the more than seventy substrate analogues were synthesized, among which MMI-005, MMI-012, MMI-017, MMI-018, MMI-025, MMI-026, MMI-037, MMI-039, MMI-040, MMI-066, MMI-070, and MMI-071 have **inhibition** constants in the range of 1.4-61.4+10.sup.-9 M against **recombinant** pro-**memapsin 2.** These **inhibitors** are useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 6 OF 9 USPATFULL on STN
AN 2003:96167 USPATFULL
TI Catalytically active **recombinant memapsin** and methods of use thereof
IN **Tang, Jordan J. N.**, Edmond, OK, United States
Lin, Xinli, Edmond, OK, United States
Koelsch, Gerald, Oklahoma City, OK, United States
Hong, Lin, Oklahoma City, OK, United States
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United States (U.S. corporation)
PI US 6545127 B1 20030408
AI US 2000-604608 20000627 (9)
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Borin, Michael; Assistant Examiner: Zhou, Shuba
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 18
ECL Exemplary Claim: 7
DRWN 21 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 2563
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2.** The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for

memapsin 2. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 7 OF 9 USPATFULL on STN
AN 2002:294717 USPATFULL
TI Catalytically active **recombinant memapsin** and methods of use thereof
IN Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
PA Oklahoma Medical Research Foundation
PI US 2002164760 A1 20021107
AI US 2001-795903 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin**

2 bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 8 OF 9 USPATFULL on STN
AN 2002:214213 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation (U.S. corporation)
PI US 2002115600 A1 20020822
AI US 2001-845226 A1 20010430 (9)
RLI Division of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP Patrea L. Pabst, Arnall Golden & Gregory, LLP, 2800 One Atlantic Center, 1201 West Peachtree Street, Atlanta, GA, 30309-3450
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2377
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the tliree dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L13 ANSWER 9 OF 9 USPATFULL on STN

AN 2002:92777 USPATFULL
TI Catalytically active **recombinant memapsin** and methods of use thereof
IN **Tang, Jordan J. N.**, Edmond, OK, UNITED STATES
Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
PI US 2002049303 A1 20020425
AI US 2001-796264 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2441
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

=> d 18 1-10 bib ab

L8 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:12489 CAPLUS
DN 134:80832
TI **Inhibitors** of **memapsin 2** and use thereof
IN Tang, Jordan J. N.; Hong, Ling; Ghosh, Arun K.
PA Oklahoma Medical Research Foundation, USA; The Board of Trustees of the University of Illinois
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000665	A2	20010104	WO 2000-US17742	20000627
	WO 2001000665	A3	20010927		
	WO 2001000665	C2	20020725		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2374346	AA	20010104	CA 2000-2374346	20000627
	AU 2000057735	A5	20010131	AU 2000-57735	20000627
	EP 1194449	A2	20020410	EP 2000-943236	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003506322	T2	20030218	JP 2001-507071	20000627
	US 6545127	B1	20030408	US 2000-604608	20000627
	EP 1496124	A1	20050112	EP 2004-9534	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002049303	A1	20020425	US 2001-796264	20010228
	US 2002164760	A1	20021107	US 2001-795903	20010228
	US 2002115600	A1	20020822	US 2001-845226	20010430
	US 2003199676	A1	20031023	US 2003-420044	20030417
	US 2004220079	A1	20041104	US 2004-773754	20040206
	US 2004167075	A1	20040826	US 2004-820953	20040408
	AU 2004202058	A1	20040610	AU 2004-202058	20040514
	AU 2004202059	A1	20040610	AU 2004-202059	20040514
PRAI	US 1999-141363P	P	19990628		
	US 1999-168060P	P	19991130		
	US 2000-177836P	P	20000125		
	US 2000-178368P	P	20000127		
	US 2000-210292P	P	20000608		
	US 2000-210306P	P	20000608		
	AU 2000-57715	A3	20000627		
	AU 2000-57735	A3	20000627		
	EP 2000-943208	A3	20000627		
	US 2000-603713	A3	20000627		
	US 2000-604608	A3	20000627		
	WO 2000-US17742	W	20000627		
	US 2000-752878	A1	20001228		
	US 2001-845226	A1	20010430		

AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Figure 1). The **inhibition** constant of OM99-2 is 1.6 x 10-9 M against **recombinant** pro-**memapsin 2**. Crystallog. of

memapsin 2 bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using com. available **software programs** and techniques familiar to those in organic chemical and enzymol., to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:12487 CAPLUS
DN 134:68049
TI Catalytically active **recombinant memapsin 2**, 3D crystal structure based **inhibitor** design, synthesis, and screening, for **Alzheimer**'s disease **treatment**
IN Tang, Jordan J. N.; Lin, Xinli; Koelsch, Gerald
PA Oklahoma Medical Research Foundation, USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000663	A2	20010104	WO 2000-US17661	20000627
	WO 2001000663	A3	20011004		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2374610	AA	20010104	CA 2000-2374610	20000627
	AU 2000057715	A5	20010131	AU 2000-57715	20000627
	EP 1196609	A2	20020417	EP 2000-943208	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003503072	T2	20030128	JP 2001-507069	20000627
	US 6545127	B1	20030408	US 2000-604608	20000627
	EP 1496124	A1	20050112	EP 2004-9534	20000627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002049303	A1	20020425	US 2001-796264	20010228
	US 2002164760	A1	20021107	US 2001-795903	20010228
	US 2002115600	A1	20020822	US 2001-845226	20010430
	US 2003199676	A1	20031023	US 2003-420044	20030417
	US 2004220079	A1	20041104	US 2004-773754	20040206
	US 2004167075	A1	20040826	US 2004-820953	20040408
	AU 2004202058	A1	20040610	AU 2004-202058	20040514
	AU 2004202059	A1	20040610	AU 2004-202059	20040514
PRAI	US 1999-141363P	P	19990628		
	US 1999-168060P	P	19991130		
	US 2000-177836P	P	20000125		
	US 2000-178368P	P	20000127		
	US 2000-210292P	P	20000608		
	US 2000-210306P	P	20000608		
	AU 2000-57715	A3	20000627		
	AU 2000-57735	A3	20000627		
	EP 2000-943208	A3	20000627		
	US 2000-603713	A3	20000627		
	US 2000-604608	A3	20000627		
	WO 2000-US17661	W	20000627		

US 2000-752878 A1 20001228
US 2001-845226 A1 20010430

AB A method for producing catalytically active **recombinant** **memapsin 2** comprising expression in a bacteria and refolding the **recombinant** **memapsin 2** under conditions which dissociate and then slowly refold the enzyme into a catalytically active form is disclosed. A method of isolating **inhibitors** of cleavage by **memapsin 2** comprising adding to one or more potential **inhibitors** of catalytically active **recombinant** **memapsin 2** , and a substrate for **memapsin 2**, and screening for decreased cleavage of the substrate by the **inhibitors**, wherein the **inhibitors** are in a library of small synthetic mols., like proteins and peptides. Alternatively, the **inhibitors** are oligonucleotides **preventing** or decreasing expression of catalytically active **memapsin 2.** A method for designing or obtaining **inhibitors** of catalytically active **memapsin 2** comprising modeling an **inhibitor** based on the crystallization coordinates of **memapsin 2** or parameters. A database comprising binding properties and chemical structures of compds. designed or screened by modeling an **inhibitor** based on the crystallization coordinates of **memapsin 2** or parameters is claimed. A method of **treating** or **preventing** **Alzheimer**'s disease comprising administering to a patient in need thereof an **inhibitor** of **memapsin 2** which binds to the active site of the **memapsin 2** defined by the presence of two catalytic aspartic residues and substrate binding cleft, is also claimed. The cDNAs of two new human membrane-associated aspartic proteases, **memapsin** 1 and **memapsin 2** , have been cloned and sequenced. The substrate and subsite specificity of the catalytically active enzyme have been determined The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2.** The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2.** The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2.** Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Fig. 1). The **inhibition** constant of OM99-2 is 1.6 x 109 M against **recombinant** pro-**memapsin** **2.** Crystallog. of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used to design new **inhibitors**, using com. available **software programs** and techniques familiar to those in organic chemical and enzymol., to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 3 OF 10 USPATFULL on STN
AN 2004:280778 USPATFULL
TI **Inhibitors** of **Memapsin 2** and use thereof
IN Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, UNITED STATES (U.S. corporation)
The Board of Trustees of the University of Illinois, Urbana, IL, UNITED

STATES (U.S. corporation)
PI US 2004220079 A1 20041104
AI US 2004-773754 A1 20040206 (10)
RLI Continuation of Ser. No. US 2001-845226, filed on 30 Apr 2001, ABANDONED
Division of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP Kenneth E. Jenkins Eqs., Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA, 94111-3834
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 4 OF 10 USPATFULL on STN
AN 2004:215966 USPATFULL
TI **Inhibitors** of **Memapsin 2** and use thereof
IN Tang, Jordan J. N., Edmond, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, UNITED STATES (U.S. corporation)
The Board of Trustees of the University of Illinois, Urbana, IL, UNITED STATES (U.S. corporation)
PI US 2004167075 A1 20040826
AI US 2004-820953 A1 20040408 (10)
RLI Continuation of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)

DT Utility
FS APPLICATION
LREP TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 5 OF 10 USPATFULL on STN
AN 2004:126971 USPATFULL
TI Crystal structure of beta site **APP** cleaving enzyme (BACE) and methods of use thereof
IN Vuillard, Laurent Michel Marie, Cambridge, UNITED KINGDOM
Patel, Sahil Joe, Cambridge, UNITED KINGDOM
Yon, Jeffrey Roland, Cambridge, UNITED KINGDOM
Cleasby, Anne, Cambridge, UNITED KINGDOM
Hamilton, Bruce John, Cambridge, UNITED KINGDOM
Shah, Aleem, Cambridge, UNITED KINGDOM
PI US 2004096950 A1 20040520
AI US 2003-627473 A1 20030725 (10)
PRAI US 2002-398681P 20020726 (60)
DT Utility
FS APPLICATION
LREP FROMMER LAWRENCE & HAUG, 745 FIFTH AVENUE- 10TH FL., NEW YORK, NY, 10151
CLMN Number of Claims: 84
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 9132
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present application discloses and claims mutant BACE proteins, **recombinant** BACE proteins, processes for crystallizing BACE and in particular to its crystal structure and to the uses of this structure in drug discovery.

L8 ANSWER 6 OF 10 USPATFULL on STN

AN 2003:134541 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN Tang, Jordan J. N., Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK (U.S. corporation)
PI US 2003092629 A1 20030515
AI US 2001-32818 A1 20011228 (10)
PRAI US 2001-275756P 20010314 (60)
US 2000-258705P 20001228 (60)
DT Utility
FS APPLICATION
LREP HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 2203
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed-, The substrate and subsite specificity of the catalytically active enzyme have been determined by a method which determines the initial hydrolysis rate of the substrates by using MALDI-TOF/MS. Alternatively, the subsite specificity of **memapsin** can be determined by probing a library of **inhibitors** with **memapsin 2** and subsequently detecting the bound **memapsin 2** with an antibody raised to **memapsin 2** and an alkaline phosphatase conjugated secondary antibody. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2.** The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2.** The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2.** Processes for the synthesis of substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the more than seventy substrate analogues were synthesized, among which MMI-005, MMI-012, MMI-017, MMI-018, MMI-025, MMI-026, MMI-037, MMI-039, MMI-040, MMI-066, MMI-070, and MMI-071 have **inhibition** constants in the range of 1.4-61.4+10.sup.-9 M against **recombinant** pro-**memapsin 2.** These **inhibitors** are useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 7 OF 10 USPATFULL on STN
AN 2003:96167 USPATFULL
TI Catalytically active **recombinant memapsin** and methods of use thereof
IN Tang, Jordan J. N., Edmond, OK, United States
Lin, Xinli, Edmond, OK, United States
Koelsch, Gerald, Oklahoma City, OK, United States
Hong, Lin, Oklahoma City, OK, United States
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United States (U.S. corporation)
PI US 6545127 B1 20030408
AI US 2000-604608 20000627 (9)
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)

DT Utility
FS GRANTED
EXNAM Primary Examiner: Borin, Michael; Assistant Examiner: Zhou, Shuba
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 18
ECL Exemplary Claim: 7
DRWN 21 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 2563
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 8 OF 10 USPATFULL on STN
AN 2002:294717 USPATFULL
TI Catalytically active **recombinant memapsin** and methods of use thereof
IN Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
PA Oklahoma Medical Research Foundation
PI US 2002164760 A1 20021107
AI US 2001-795903 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed.

The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 9 OF 10 USPATFULL on STN
AN 2002:214213 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation (U.S. corporation)
PI US 2002115600 A1 20020822
AI US 2001-845226 A1 20010430 (9)
RLI Division of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP Patrea L. Pabst, Arnall Golden & Gregory, LLP, 2800 One Atlantic Center, 1201 West Peachtree Street, Atlanta, GA, 30309-3450
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2377
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1

and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the tliree dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L8 ANSWER 10 OF 10 USPATFULL on STN
AN 2002:92777 USPATFULL
TI Catalytically active **recombinant memapsin** and methods of use thereof
IN Tang, Jordan J. N., Edmond, OK, UNITED STATES
Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
PI US 2002049303 A1 20020425
AI US 2001-796264 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2441
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6+10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to

design new **inhibitors** to **memapsin 2**,
useful in **diagnostics** and for the **treatment** and/or
prevention of **Alzheimer**'s disease.

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---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 19:18:08 ON 07 JUN 2006